

## (12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
5 August 2004 (05.08.2004)

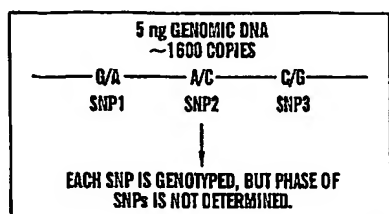
PCT

(10) International Publication Number  
**WO 2004/065617 A2**

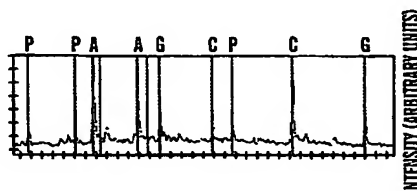
- (51) International Patent Classification<sup>7</sup>: C12Q
- (21) International Application Number: PCT/US2004/001329
- (22) International Filing Date: 16 January 2004 (16.01.2004)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data: 60/441,046 17 January 2003 (17.01.2003) US
- (71) Applicant (for all designated States except US): **THE TRUSTEES OF BOSTON UNIVERSITY** [US/US]; One Sherborn Street, Boston, MA 02218 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): **CANTOR, Charles,**
- R. [US/US]; 526 Stratford Court, Del Mar, CA 92014 (US). **DING, Chunming** [CN/US]; 10-C Sagamore Way, Waltham, MA 02453 (US).
- (74) Agents: **EISENSTEIN, Ronald, I.** et al.; Nixon Peabody LLP, 100 Summer Street, Boston, MA 02110 (US).
- (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),

[Continued on next page]

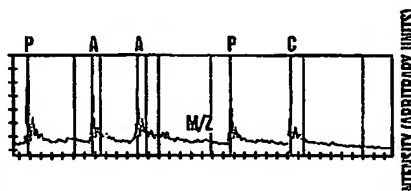
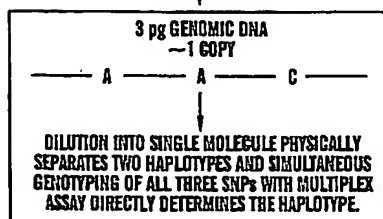
(54) Title: **HAPLOTYPE ANALYSIS**



DILUTION  
TO  
**FIG. 1B**

**A**

FROM  
**FIG. 1A**  
DILUTION

**B**

**(57) Abstract:** The present invention provides an efficient way for high throughput haplotype analysis. Several polymorphic nucleic acid markers, such as SNPs, can be simultaneously and reliably determined through multiplex PCR of single nucleic acid molecules in several parallel single molecule dilutions and the consequent statistical analysis of the results from these parallel single molecule multiplex PCR reactions results in reliable determination of haplotypes present in the subject. The nucleic acid markers can be of any distance to each other on the chromosome. In addition, an approach wherein overlapping DNA markers are analyzed can be used to link smaller haplotypes into larger haplotypes. Consequently, the invention provides a powerful new tool for diagnostic haplotyping and identifying novel haplotypes.



Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

**Published:**

- *without international search report and to be republished upon receipt of that report*